**MESA Exam 6 Ancillary Study 253 Data Set Variable Guide**

Brain MRI – Mean Free Water in White Matter

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| **Data Set name :** | MESAe6as253\_BMRIFW\_20240423 |
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**MESA Ancillary study #253, Atrial Fibrillation Study**

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See ancillary study publications1-3 in the Reference list below for information on ancillary study methods and for examples of how to analyze the brain MRI data. Please acknowledge the Atrial Fibrillation Ancillary Study funding in all publications that use these brain MRI data, as follows:

“Brain MRI acquisition and analysis was supported by R01 HL127659 from the National Heart, Lung, and Blood Institute with additional support from the National Institute on Aging.”

MESA participants from all six field centers who participated in the Atrial Fibrillation ancillary study2 at Exam 6 were invited to complete a 3T brain MRI a median 18 (IQR: 16, 20) months after the Exam 6 visit. This data set contains one record per ancillary study participant (n=1062) who completed a brain MRI in March 2018 through August 2019 as part of the Atrial Fibrillation ancillary study.

Drs. Tanweer Rashid and Mohamad Habes at the University of Texas Health Science Center San Antonio provided this dataset of Mean Free Water Fraction in White Matter. Free water is calculated from diffusion weighted MRI using a two-compartment tensor model. One compartment is the free water compartment which models the isotropic diffusion with a diffusion coefficient of water at body temperature of 37° C, fixed to 3 × 10−3 mm2/s. The other compartment accounts for all other molecules (intra- and extracellular) that are hindered or restricted by tissue membranes.4 The mean free water in white matter variable is expressed as a proportion (between 0 and 1) reflecting the proportion of extracellular water in the voxel, with higher values indicating greater free water content. Greater free water content in white matter has recently been identified as a sensitive and early biomarker of white matter injury in association with vascular risk factors5 and cognitive impairment.6 Mean free water in white matter was quantified on these MRI scans using the open source kit from the MARKVCID consortium: <https://markvcid.partners.org/sites/default/files/markvcid2/protocols/MarkVCID_FW_Kit_Protocol_v6.12.23.pdf>

Recommended exclusions:

Of the 1062 participants with brain MRI, two participants have no data on mean free water in white matter and have missing data for that variable.

Recommended adjustments: All brain MRI analyses in MESA should be adjusted for field center.

**References**

1. Austin TR, Nasrallah IM, Erus G, Desiderio LM, Chen LY, Greenland P, Harding BN, Hughes TM, Jensen PN, Longstreth WT, Jr., et al. Association of Brain Volumes and White Matter Injury With Race, Ethnicity, and Cardiovascular Risk Factors: The Multi-Ethnic Study of Atherosclerosis. *Journal of the American Heart Association*. 2022;11:e023159. doi: 10.1161/JAHA.121.023159

2. Heckbert SR, Austin TR, Jensen PN, Chen LY, Post WS, Floyd JS, Soliman EZ, Kronmal RA, Psaty BM. Differences by race/ethnicity in the prevalence of clinically detected and monitor-detected atrial fibrillation: MESA. *Circulation Arrhythmia and electrophysiology*. 2020;13:e007698. doi: 10.1161/CIRCEP.119.007698

3. Charisis S, Rashid T, Dintica C, Gonzales M, Liu H, Ware JB, Austin TR, Jensen PN, Fohner AE, Tanley JE, et al. Spatial Heterogeneity of Brain MRI Markers of Small Vessel Disease and Cognition. (under review).

4. Pasternak O, Sochen N, Gur Y, Intrator N, Assaf Y. Free water elimination and mapping from diffusion MRI. *Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine*. 2009;62:717-730. doi: 10.1002/mrm.22055

5. Maillard P, Mitchell GF, Himali JJ, Beiser A, Fletcher E, Tsao CW, Pase MP, Satizabal CL, Vasan RS, Seshadri S, et al. Aortic Stiffness, Increased White Matter Free Water, and Altered Microstructural Integrity: A Continuum of Injury. *Stroke*. 2017;48:1567-1573. doi: 10.1161/STROKEAHA.116.016321

6. Ji F, Pasternak O, Liu S, Loke YM, Choo BL, Hilal S, Xu X, Ikram MK, Venketasubramanian N, Chen CL, et al. Distinct white matter microstructural abnormalities and extracellular water increases relate to cognitive impairment in Alzheimer's disease with and without cerebrovascular disease. *Alzheimers Res Ther*. 2017;9:63. doi: 10.1186/s13195-017-0292-4

| **Order** | **Variable** | **Variable Description** |
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| 1 | idno | MESA Participant ID |
| 2 | agebrainmri6c | Age at exam 6 brain MRI |
| 3 | brainmri\_tt6c | Time from baseline to exam 6 brain MRI (days) |
| 4 | mean\_fw\_in\_wm | Mean free water in white matter |